I.10 Systemic therapy

Opmeer BC, Heydendael VMR, de Borgie CAJM et al. Costs of treatment in patients with moderate to severe plaque psoriasis: economic analysis in a randomized controlled comparison of methotrexate and cyclosporine. *Arch Dermatol.* 2004; 140(6):685-690. Ref ID: OPMEER2004				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost minimisation analysis **Study design:** Trial-based analysis **Approach to analysis:** Assumed equal efficacy between methotrexate and ciclosporin and used prospectively collected resource data to compare costs of 16-week treatment and 36-week follow-up. **Perspective:** Dutch society (but only direct medical costs reported here) **Time horizon:** 1 year (16 weeks treatment; 36 weeks follow-up) **Treatment effect duration:** NA **Discounting:** NA	**Population:** Patients with moderate to severe plaque psoriasis **Cohort settings:** Mean age = 41.6 (13) MTX; 38.3 (12.4) Cyclosp M = 65% MTX; 69% Cyclosp **Intervention 1:** Methotrexate, 16 weeks treatment **Intervention 2:** Ciclosporin, 16 weeks treatment	**Total costs (mean per patient):** Intvn 1: £1,934 Intvn 2: £2,410 Incremental(2-1): -£476 (CI NR; p=NR) **Currency & cost year:** 1999 Dutch Euros (presented here as 1999 UK pounds‡) **Cost components incorporated:** Medication, outpatient visits, comedication during follow-up, diagnostic and laboratory tests, additional visits to health care providers. *Direct non-medical and indirect costs were reported but have been excluded from the data reported here	**Primary outcome measure:** Effectiveness between treatments assumed to be equal	**Cost minimisation analysis** (If effectiveness of methotrexate and ciclosporin is equal): Methotrexate has lower overall costs; therefore, methotrexate is cost-saving compared to ciclosporin. **Analysis of uncertainty:** Visual inspection of box and whisker plots indicates that costs accrued during treatment were significantly different between strategies, but this did not hold during 36 weeks follow-up.

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Data sources
Health outcomes: Analysis was performed prospectively as part of the RCT comparing methotrexate and ciclosporin conducted by Heydendael 2003{Heydendael, 2003 HEYDENDAEL2003 /id}. **Quality-of-life weights:** NA **Cost sources:** Resource data was collected prospectively as part of the RCT. Patients were seen every other week during the first month and every 4 weeks in the subsequent 12 weeks of treatment and 36 weeks of follow-up. Clinical (PASI), functional (SF-36) and economic (resource utilisation) outcomes were measured at each visit. Unit prices were based on previous estimates{de Rie, 2001 DERIE2001 /id}, Dutch pharmaceutical cost listings, guideline prices and national tariffs.
Comments
Source of funding: Dutch Health Insurance Board **Limitations:** Short time horizon (1 year); relatively old cost estimates (1999/2000); no sensitivity analysis reported; costing perspective is Dutch society: some uncertainty about applicability of Dutch estimates of resource use and unit costs; cost-minimisation method **Other:**
Overall applicability*: Partially applicable **Overall quality**:** Potentially serious limitations

Abbreviations: NR = not reported ‡ Converted using 2006 Purchasing Power Parities Organisation for Economic Co-operation and Development (OECD). OECD Stat Extracts: purchasing power parities for GDP. http://stats oecd org/Index aspx?datasetcode=SNA_TABLE4 [2010 [accessed2011 Feb 24]
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

Sizto S, Bansback N, Feldman SR et al. Economic evaluation of systemic therapies for moderate to severe psoriasis. Br J Dermatol. 2009; 160(6):1264-1272. Ref ID: SIZTO2009				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost utility analysis **Study design:** Decision analytic model **Approach to analysis:** The model separately examines a trial period and a treatment	**Population:** Patients with moderate to severe psoriasis **Cohort settings:** Start age = not stated M = not stated **Intervention 1:**	**Total costs (mean per patient):** Intvn 1: Not reported Intvn 2: Not reported Incremental(2-1): £1,857 (CI £1,736, £2,125 ; p=NR) **Currency & cost year:** 2005/06 UK pounds	**Primary outcome measure:** QALYs (mean per patient) Intvn 1: 0.129 Intvn 2: 0.079 Incremental (2-1): - 0.05 (CI -0.034, -0.069; p=NR)	**Primary ICER (Intvn 2 vs Intvn 1):** Methotrexate dominates ciclosporin Probability cost-saving: approximately 80% (pa) **Analysis of uncertainty:** One way sensitivity analyses around assumed weight of patient (60 kg), increased response rates and higher dosage of ciclosporin do not change results.

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period. Only responders during the trial period continue treatment and at a later point they may withdraw due to loss of efficacy or toxicity **Perspective:** UK NHS **Time horizon:** not stated **Treatment effect duration:** Assumed to maintain response achieved at the end of trial **Discounting:** Not stated	Methotrexate (15-25 mg/wk, 16 weeks treatment) **Intervention 2:** Cyclospoine (3 mg/kg/day for 80 kg patient, 12 weeks treatment)	**Cost components incorporated:** Medications, monitoring and inpatient visits; cost of dermatology outpatient visits and GP visits excluded		
Data sources				
Health outcomes: Short term efficacy of treatments was determined through a systematic review and network meta-analysis, described in full by Bansback and colleagues{Bansback, 2009 BANSBACK2009 /id}. No estimates, sources or assumptions reported for the longer term treatment parameters. **Quality-of-life weights:** EQ-5D weights were attached to responder (moderate (≥PASI50 to <PASI90) and good (≥PASI90)) and non-responder (<PASI50) health states. Weights based on data from the CHAMPION{Saurat, 2008 SAURAT2008 /id} and REVEAL (Menter 2008) trials. **Cost sources:** Unit costs of drugs were taken from the British National Formulary 2007. Unit costs for laboratory tests and outpatient visits for the administration of drugs were taken from Woolacott and colleagues{Woolacott, 2006 WOOLACOTT2006 /id} and the NHS Reference Costs and National Tariff (2004). Out of date costs were inflated using the PSSRU inflation index.				
Comments				
Source of funding: Abbott Laboratories **Limitations:** Time horizon not stated; estimates of long-term effectiveness/withdrawal of treatments not stated; excludes important costs of outpatient dermatology and GP visits; funded by Abbott laboratories (makers of Adalimumab – biologic therapy included in the analysis); no discounting rates reported for costs or effects **Other:**				
Overall applicability*: Directly applicable **Overall quality**:** Potentially serious limitations				

Abbreviations: CI = confidence interval; ICER = incremental cost-effectiveness ratio; NR = not reported; pa = probabilistic analysis
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

Woolacott N, Hawkins N, Mason A et al. Etanercept and efalizumab for the treatment of psoriasis: a systematic review. Health Technol Assess. 2006; 10(46):1-iv. Ref ID: WOOLACOTT2006				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost utility analysis **Study design:** Decision analytic model **Approach to analysis:** The model separately examines a trial period and a treatment period. Only responders during the trial period continue treatment and at a later point they may withdraw due to loss of efficacy or toxicity **Perspective:** UK NHS **Time horizon:** up to 10 years **Treatment effect duration:** Assumed to maintain response achieved at the end of trial **Discounting:** Costs: 6%; Outcomes: 1.5%	**Population:** Patients with moderate to severe chronic plaque psoriasis **Intervention 1:** Methotrexate (10-25 mg/wk, 16 weeks treatment) **Intervention 2:** Ciclosporin (2.5-5 mg/day, 12 weeks treatment)	**Total costs (mean per patient):** Intvn 1:Not reported Intvn 2: Not reported Incremental(2-1): £3,771 (CI £3265,£3,809; p=NR) **Currency & cost year:** 2004/05 UK Pounds **Cost components incorporated:** Direct NHS costs only: drugs and their administration, monitoring, outpatient visits and inpatient stays	**Primary outcome measure:** QALYs (mean per patient) Intvn 1: 0.126 Intvn 2: 0.122 Incremental (2-1): -0.004 (CI 0, -0.007; p=NR)	**Primary ICER (Intvn 2 vs Intvn 1):** Methotrexate dominates ciclosporin Probability most cost-effective: 100% **Analysis of uncertainty:** Evaluation of methotrexate and ciclosporin was part of a sensitivity analysis to an analysis focused on the evaluation of two biologics, etanercept and efalizumab. In this sensitivity analysis, both methotrexate and ciclosporin were cost-saving compared to 'best supportive care and all biologics except for infliximab, which was not cost-effective.
Data sources				

Woolacott N, Hawkins N, Mason A et al. Etanercept and efalizumab for the treatment of psoriasis: a systematic review. Health Technol Assess. 2006; 10(46):1-iv. Ref ID: WOOLACOTT2006
Health outcomes: Short term efficacy of treatments was determined through a systematic review and network meta-analysis, described in full within the same report. Estimates of longer term treatment duration were based on an assumed annual drop-out rate for responding patients receiving treatment and a maximum assumed treatment period based on published guidelines (Griffiths 2004; Sterry 2004) if appropriate. Mean length of treatment response was then estimated from a 10-year Markov model with annual cycles. **Quality-of-life weights:** Health state utilities were estimated from an analysis of data from three etanercept regulatory trials and the HODaR Database (http://www.hodar.co.uk/). The estimates process consisted of 2 stages. First, the mean change in DLQI score between basely and week 12 was estimated for patients from etanercept trials with different levels of PASI response and different baseline DLQI scores. This analysis was facilitated by access to patient-level data by Wyeth but is commercial in confidence. Data within the HODaR database included patients who had completed both the DLQI and EQ-5D. These data were used to 'map' the change in DLQI associated with PASI responses to changes in EQ-5D utility. An ordinary least-squares linear regression analysis of the DLQI-EQ-5D data from HODaR allowed for the calculation of an algorithm (commercial in confidence). Based on these data, the mean gain in utility was estimated for the various PASI response categories (<PASI50, ≥PASI50 to <PASI75, ≥PASI75 to <PASI90, and ≥PASI90). **Cost sources:** Drug dosage and titration rates were based on the British National Formulary. Several sources were used to inform the estimates of types and frequency of laboratory tests. No published data were available to inform an estimate of the rate of hospitalisation, so estimates were based on a range of scenarios informed by expert opinion. Length of stay for an inpatient admission was based on Department of Health Hospital Episode Statistics for psoriasis and supported by evidence from recently conducted audits. Frequency of liver biopsy was based on estimates from a recent economic evaluation{Chalmers, 2005 CHALMERS2005 /id}. Expert opinion was used to generate the frequency of outpatient visits, drug tablet sizes, monitoring requirements and titration rates not available in the literature. Prices were taken from the BNF where available. Prices of monitoring tests were obtained from the Biochemistry Department at York NHS Trust. Outpatient visits were based on the NHS Reference Cost category 'Other attendance with other investigation or procedure.' The cost of an inpatient day was based on an average of 'Elective inpatient HRG data, major dermatological conditions J39' and 'Elective inpatient HRG data, major dermatological conditions J40.' Where necessary, costs were updated to 2003-04 using the PSSRU inflation index.
Comments
Source of funding: NHS R&D HTA Programme **Limitations:** Analysis was mainly focused on evaluation of etanercept and efalizumab – ciclosporin and methotrexate were evaluated as part of one probabilistic scenario analysis; discounting rates were 6% for costs and 1.5% for benefits instead of 3.5% for both **Other:** This was the economic analysis underpinning NICE Technology Appraisal 103, guidance on the use of etanercept and efalizumab.
Overall applicability*: Directly applicable **Overall quality**:** Minor limitations

Abbreviations: CI = confidence interval; ICER = incremental cost-effectiveness ratio; NR = not reported; pa = probabilistic analysis
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*